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Encapsulation systems for the delivery of hydrophilic nutraceuticals: food application

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Abstract

Increased health risk associated with the sedentary life style is forcing the food manufacturers to look for food products with specific or general health benefits e.g. beverages enriched with nutraceuticals like catechin, curcumin rutin. Compounds like polyphenols, flavonoids, vitamins are the good choice of bioactive compounds that can be used to fortify the food products to enhance their functionality. However due to low stability and bioavailability of these bioactives (both hydrophobic and hydrophilic) within the heterogeneous food microstructure and in the Gastro Intestinal Tract (GIT), it becomes extremely difficult to pass on the real health benefits to the consumers.

Recent developments in the application of nano-delivery systems for food product development is proving to be a game changer which has raised the expectations of the researchers, food manufacturers and consumers regarding possibility of enhancing the functionality of bioactives within the fortified food products. In this direction, nano/micro delivery systems using lipids, surfactants and other materials (carbohydrates, polymers, complexes, protein) have been fabricated to stabilize and enhance the biological activity of the bioactive compounds.

In the present review, current status of the various delivery systems that are used for the delivery of hydrophilic bioactives and future prospects for using other delivery systems that have been not completely explored for the delivery of hydrophilic bioactives e.g. niosomes; bilosomes, cubosomes are discussed.

Keywords: Hydrophilic, bioactives, nanoparticles, stability, bioavailability, food, delivery.

1.Introduction

In the last decade, the effect of specific food on general wellbeing has gained more importance among the consumers. These food products are usually termed as functional foods or fortified foods (Aditya and Ko, 2015; Lam et al., 2014). This has opened the opportunity for the food industries to market the food products with general or specific health benefits (Day et al., 2009; Lam et al., 2014).

In the current scenario, several approaches have been made to add healthy functionalities to the food products e.g. altering their microstructure or composition i.e., designing the specific microstructured food products to obtain the release of nutrients or functional ingredients at specific parts of the GIT, use of nano/micro carriers to add specific bioactives to the food products to protect them from degradation, reducing the fat, salt in the product to minimize the calorie intake.

With regard to the food fortification, food products are normally fortified with health promoting and disease preventing generally recognized as safe (GRAS) approved food grade nutrients and bioactives such as phytochemicals, vitamins, minerals, oils (omega 3 fatty acids). These molecules are obtained from a wide range of plants, animals, and microbes of both terrestrial and aquatic inhabitants (Venugopal, 2008; Zhu et al., 2013). However, the formulation and delivery of bioactives in the complex food products poses substantial challenges owing to their unfavourable physicochemical characteristics. The major problems associated with addition of bioactive molecules directly to the product are; their bitter and astringent taste and degradation of ingredients when exposed to unfavorable conditions during processing (temperature, pressure) and storage (presence of oxygen, temperature and light) (Bandyopadhyay et al., 2012; Rothwell et al., 2015; Smuda and Glomb, 2013; Wang et al., 2008). These conditions lead to unwanted changes in the product physico-chemical stability, organoleptic properties e.g. color, taste, appearence (Aditya and Ko, 2015; Cheynier, 2005; McClements, 2015; Velikov and Pelan, 2008; Zorić et al., 2016). Further problem is that, due to unfavorable environment present in the GIT e.g. the wide range and fluctuation in pH, presence of various enzymes and mucosal barrier etc., bioactives have a very low bioavailability, bioaccessibility and membrane permeability. Consequently at the end, this gives rise to a loss in the commercial value and biological activity of the food product(Mirafzali et al., 2014).

In recent years, several strategies have been developed to increase the stability of bioactives during product development, storage and consumption such as

a. Colloidal carrier systems with varied physicochemical properties such as size, shape, surface characteristics, stability, and carrier materials(Velikov and Pelan, 2008).
b. Specialized manufacturing and storage techniques like freeze-drying, spray drying, microwave drying (Fang and Bhandari, 2012)
c. Use of bioenhancers like piperine in combination with other bioactives e.g. use of piperine increases bioavailability of curcumin by inhibiting glucuronidation in the intestine(Shoba et al., 1998).

Recent advancements in nano/micro delivery technology that originated from the pharmaceutical technology have been increasingly investigated to overcome the drawbacks associated with the direct incorporation of functional ingredients into food products(Aditya et al., 2015b; Aditya et al., 2014; Patel and Velikov, 2011). In this respect, over the last decade various types of materials like fats, polymers, lipid-polymer conjugates, proteins, carbohydrates have been used as carrier materials and usually more than 2000 research papers are published annually by scientists both from industry and academia with regarding to application of nanocarriers for food

fortification(Patel and Velikov, 2011; Yao et al., 2015). However, most of these delivery systems are designed to deliver hydrophobic bioactives(McClements et al., 2016; McClements and Xiao, 2014). The main reason is the source of originality of the nano/micro delivery systems. Nano/micro delivery systems like liposomes, solid lipid nanoparticles (SLN) and polymeric nanoparticles are designed to deliver hydrophobic pharmaceutical agents with low bioavailability. In pharmaceutical science, delivery of hydrophilic drug molecules are less challenging due to the possibility of formulating the dosages in various forms e.g. if drug molecules are unstable in the aqueous phase after formulation they can be converted into tablets or capsules. However, such modification of food product is not accepted since they change the aesthetic and organoleptic properties of the product that takes away the pleasure of eating. Hence developing a tailor made delivery systems that can protect the bioactives from degradation during product development, storage and consumption and also keep the original aesthetic and organoleptic property of the fortified food product intact is highly required.

This review article will emphasize nano/micro delivery systems that have been used in food products to deliver the nutrients or active ingredients (bioactives), which have documented health benefits. Information regarding other approaches that can be used to provide the functionality to the food products can be obtained by reading other review articles(Gregersen et al., 2015; Norton et al., 2015).

2. Need for colloidal delivery system for hydrophilic molecules

The major challenges for the development of food products fortified with hydrophilic molecules are their physical and chemical susceptibility within the complex food matrix. Here we explain the need for suitable delivery systems for food fortification at various stages of product development and marketing.

2.1. Low bioavailability

In general, bioavailability is compromised in hydrophobic molecules due to their low aqueous solubility. However, in certain instances, where hydrophilic molecules have high molecular weight, irreversible binding of hydrophilic molecules with proteins in the GIT, degradation of molecules before reaching their active adsorption site due to different environment e.g. pH, enzyme composition, ionic strength etc., within the GIT compromises their bioavailability. Some of the hydrophilic nutraceuticals that require delivery systems to overcome the bioavailability problems are polyphenols (quercetin, catechin), proteins and peptides (Aditya et al., 2015b). This necessitates colloidal delivery system for hydrophilic molecules.

2.2. Product development

In general, instability during product development occurs due to chemical instability and physical instability. However, both are interrelated and lead to product destabilization.

Often the food matrix contains ingredients with varying physicochemical properties. High solubility of hydrophilic bioactive compounds increases their interaction with co-ingredients such as oxidizing and reducing agents, transition metals, hydrogen ions which stimulate their chemical degradation Further, some of the bioactives like ascorbic acid, catechin, anthocyanins are highly susceptible to conditions like high temperature, presence of oxygen and light. Since, during product development ingredients are exposed to various extreme conditions e.g. thermal sterilization, high-pressure mixing and blending etc., bioactives undergo rapid oxidation, hydrolysis,

reduction which results in their degradation or less active by-product formation(Aditya et al., 2015a).

Another important factor is the presence of multiple ingredients within the food matrix with different physicochemical properties e.g. presence of hydrophobic molecules like lipids. Feasibility of adding hydrophilic bioactive to lipid-enriched products like margarine and butter depends mainly on two factors i.e. solubility of the hydrophilic compound in the lipid phase and water phase. If solubility is less in water, then the total amount of bioactives that can be added is very limited compared to food products, which contains higher proportion of water e.g. beverages, soup. Similarly, if the hydrophilic bioactives even have the slightest solubility in lipid, then that compromises products physico-chemical stability and sensorial properties due mass transfer of bioactives from one region to another (McClements, 2015; Patel and Velikov, 2011; Velikov and Pelan, 2008). Thus, to fortify the lipid-enriched products, hydrophilic bioactives should have extremely low solubility in the lipid phase (to avoid mass transfer) and very high solubility in water (to entrap more bioactives).

2.3. Obtaining the consumer and regulatory acceptance

Some of the bioactive molecules induce undesired organoleptic properties to the food products e.g. addition of catechin causes bitterness, addition of ascorbic acid induces sour or tart taste. These undesired changes compromises the consumer acceptability(Drewnowski and Gomez-Carneros, 2000). Further, since most of these bioactives are highly susceptible for degradation in GIT, after consumption, major portion of the bioactives are degraded e.g. catechin stability decreases in the presence of oxygen, alkaline pH, and high temperature and also it has low cellular permeability. Thus, the fortified food products fail to pass on the real health benefits associated with these bioactives consumption(Janaswamy and Youngren, 2012; McClements et al., 2009). Thus obtaining consumer and regulatory acceptance becomes a major hurdle.

3. Delivery systems for hydrophilic bioactives

Though several GRAS approved materials like lipids, polymers, carbohydrates, proteins can be used to fabricate nano/micro carrier, only a few of them are suitable for regular consumption. . Among the materials that can be used to fabricate carrier structures for the delivery of hydrophilic bioactives are: polysaccharides (pectin, gum arabica, carrageenan, chitosan), polymers (poly(lactic-*co*-glycolic acid), Poly(organophosphazene), Poly(lactic acid)), lipids (phospholipids, fatty acids), proteins (whey protein, soy proteins, casein) and surfactants (polysorbates, soy or egg lecithin). In general, a tailor made approach is required to design the delivery system that are suitable for the specific bioactive compounds depending on the physicochemical characteristics such as solubility, chemical interaction, shelf life etc. In addition there are other formulation factors that need to be considered based on the final application such as the amount of bioactive required to be added, storage conditions, shelf life of the product, type of food product (Patel and Velikov, 2011). In this respect, some of the delivery systems, which have been developed for the encapsulation of hydrophilic bioactives with potential for targeted and controlled delivery are discussed below.

3.1. Lipid Based Delivery Systems

3.1.1. Double emulsions (Duplex or Multiple emulsions)

Double emulsions are one of the most advanced functional microstructures. Double emulsions are constructed by using both water in oil (W/O) and oil in water (O/W) emulsion. During double emulsion fabrication, generally a two-step emulsification process is adopted. In the first step (primary emulsification), water in oil (W1/O) emulsion is fabricated and usually it is termed as primary emulsion. In the secondary emulsification step, water in oil in water (W1/O/W2) emulsion is fabricated using the primary emulsion (W1/O) as the oil phase in a second water phase W2.

Usually, secondary emulsification process is generally carried out in a lesser shear condition compared to the primary emulsification process in order to prevent the rupture of the primary emulsion.

Since these complex structures contain both oil (O) and water phases (W1 and W2), they can be used to entrap and deliver both hydrophilic and hydrophobic bioactives unperceivably (Figure 1). In recent years, these structures have been extensively explored to fortify the food products with various bioactives e.g. to protect probiotics in the acidic stomach condition and to ensure their delivery to the intestine (mainly gut) (Pimentel-González et al., 2009), for the entrapment of vitamins and minerals to avoid their degradation in the product(Bonnet et al., 2009; Bou et al., 2014),to obtain controlled or prolonged release of entrapped compounds e.g. xylitol was encapsulated in the core of a double emulsion (W1) and incorporated into the chewing gum matrix to obtain the prolonged release of Xylitol to provide sweet mouth feel for a longer period (Santos et al., 2015). Encapsulation of *Lactobacillus rhamnosus* within the double emulsion increased their survivality in acidic pH and bile salts from 71% and 89% to 108% and 128%. They have been also used to fortify beverages with both hydrophilic (catechin) and hydrophobic (curcumin) bioactives. Encapsulation resulted in enhanced stability of curcumin (~50%) and catechin (~20%) in the model beverage system. This has enabled the co-delivery of nutraceuticals that require to act synergically to augment their therapeutic and health promoting potential (Aditya et al., 2015b).Further, double emulsions have been investigated as the potential structures to reduce fat and salt in the liquid and semi-solid foods without altering the native sensory properties of the food products (Frasch-Melnik et al., 2010; Lad et al., 2012).

Although, several research reports about their formation, stability, encapsulation potential and release have been published, only a few attempts have been made towards incorporating these structures in the industrially processed food products. In this context, only one study has been reported where the internal water phase (W1) of the double emulsion has been used to entrap hydrophilic vitamin B12 and then these double emulsions were used to manufacture cheese. These system has showed excellent encapsulation efficiency and protected vitamin B12 from degradation in the acidic condition of the stomach(Giroux et al., 2013).

Though, these structures offer a variety of possibilities, their complex structure makes their production and stabilization more difficult. There appear to be two main limitations for their application into real food systems. One is their poor stability and the second one is the lack of food-grade emulsifiers that can be used for their stabilization. Due to the presence of two oppositely- curved interfaces in a single structure, both hydrophilic and hydrophobic emulsifiers are required for their stabilization. However, due to the proximity of the two oppositely curved interfaces (oil and water and water and oil), the emulsifier generally diffuses across to the opposite interface. This makes them thermodynamically unstable which subsequently destabilize the structure to form the simple emulsion (Ostwald ripening). Added to this, the chemical potential and Laplace pressure that exists within the heterogeneous

food matrix, escalates the destabilization. These technological issues can be tackled by using emulsifiers like Polyglycerol polyricinoleate (PGPR). This hydrophobic emulsifier when used in the fabrication of primary emulsion stabilizes the water and oil interfaces (W1/O) by forming a gel like structure at the interface. Nonetheless the use of PGPR in comestible products is highly regulated due to their unpleasant taste and toxicity (Dickinson, 2015a; Raoufi et al., 2012; Smith et al., 1998; Wilson et al., 1998).

To overcome this, recently emulsifiers are replaced with Pickering particles as stabilizing agents. Pickering emulsions i.e. emulsion stabilized with Pickering particles through steric stabilization has received a great interest in recent years. Solid Particles that exhibit good wettability are adsorbed at the water and oil interface providing a steric barrier that prevents coalescence. Their adsorption at the interface is known to be irreversible which helps to avoid the diffusion of particles to the respective other interfaces. The high resistance to coalescence in addition to the "surfactant-free" character makes them very attractive for their use in double emulsions. Thus, enormous research effort have been dedicated towards finding the novel food grade Pickering particles (Berton-Carabin and Schroën, 2015). In the last decade, several particles obtained from various sources e.g. plants, microorganisms synthetic particles have been used as Pickering stabilizers. Few examples are fat crystals, aggregated colloids, insoluble flavonoids, cellulose, ethyl cellulose complexes, starch granules, cocoa particles, microgels (soft particles). In one of such studies, Pickering stabilized double emulsion was fabricated using fat crystals as hydrophobic surfactant to stabilize W1/O and silica particles as hydrophilic surfactant to stabilize O/W2 emulsion(Fathi et al., 2012; Garrec et al., 2012). Moreover, recently it has been shown that soft microgels can be used as Pickering particles to stabilize the double emulsion. Here these microgel particles can be used for dual purpose. First, they can be used to stabilize the emulsion. Furthermore, the core of the microgel can be used to entrap bioactives(Dickinson, 2015b; Shewan and Stokes, 2013). However, their application in the industrially processed food products still needs to be explored.

3.1.2. Liposomes

Liposomes are the tiny globular concentric bilayer structures with an aqueous core. Liposomes are constituted using relatively biodegradable, nontoxic, biocompatible, low immunogenic phospholipids(Singh et al., 2012). These phospholipids contain hydrophilic (polar) head and hydrophobic (non polar) fatty acid tail. Various physiochemical characteristics such as size, number of bilayers or fabrication method have been used to classify them into different categories(Aditya et al., 2012; McClements, 2015; Singh et al., 2012). Depending on the number of bilayers present within the single liposome, they are classified as; unilamellar liposome vesicles (ULV) containing a single bilayer or multilamellar liposome vesicles (MLV) containing two or more bilayers. Depending on size, they are classified as small unilamellar liposome vesicles (SUV) which are ~20-100 nm, large unilamellar liposome vesicles (LUV) which are ~10 microns in size. Further depending on the number of vesicles within the single concentric bilayer structure they were classified as mono vesicular liposomes (MVL) with single vesicle or multi-vesicular liposomes (ML) with several vesicular structures entrapped within a single large vesicle(Akbarzadeh et al., 2013; Karewicz et al., 2013). Different structures of liposomes are depicted in Figure 2.

The major advantage of liposomes for the delivery of hydrophilic bioactives is the presence of inner aqueous phase. This allows higher bioactive loading (higher loading

efficiency) compared to other lipid-based delivery systems like solid lipid nanoparticles and emulsions, which lacks the aqueous inner compartments. However, there are a couple of aspects that need to be taken into account before designing the delivery system for hydrophilic as well as hydrophobic bioactives such as the amount of carrier material required to entrap the required amount of bioactives and the stability of the structures formed in the GIT.

Mouth feel (taste) and appearance of any food products depends on its ingredients composition and individual ingredient quantity. Thus excessive use of carrier material may change the mouth feel and appearance of the food products(Saha and Bhattacharya, 2010). Further, use of expensive and excessive carrier materials may also result in unfavorable cost to benefit ratio(Aditya et al., 2015c). Hence it is important to minimize the use of carrier materials. In this concern, among various types of liposomes, MLVs are best suited to protect the internalized bioactives from degradation due to the presence of multiple layers of phospholipid molecules. The presence of multiple layers increases the mechanical and chemical stability and can result in controlled release of the entrapped bioactives. However, these structures contain limited internal aqueous volume and hence limited hydrophilic bioactives can be loaded within these structures. In contrast, unilamellar liposome contains significant amount of internal aqueous phase. Hence they have the capacity to hold large quantities of hydrophilic bioactives within the core. Therefore, large unilamellar liposome seems to be more effective and best suited for hydrophilic bioactive delivery with the minimum use of carrier material(Watwe and Bellare, 1995).

Drawback that limits their use in the commercial products is their low physical and chemical stability. Liposomes are prone for degradation within the complex food matrix after interaction with co-ingredients and have limited stability in acidic condition of GIT. Oxidation of unsaturated acyl chains and hydrolysis of ester bonds are the main causes for chemical degradation that compromise their structural integrity leading to bioactive leakage(Gibbs et al., 1999). Further, their degradation increases in the acidic stomach pH, presence of pancreatic juice and bile acids (Chen and Langer, 1998; Hussain et al., 2001; Singh et al., 2012). This compromises the ability of liposomes to protect the bioactives within the GIT.

In order to, increase the stability of liposomes in these adverse conditions, several alternative routes have been explored such as addition of high amounts of hydrogenated lipids and cholesterol, coating liposome surface with polymers like chitosan, fluorinated lipids etc.,(Lian and Ho, 2001; Mady and Darwish, 2010; McIntosh et al., 1996; Reineccius, 1995). Similarly saturated lipids like dipalmitoyl phosphatidylserine (DPPS), dipalmitoyl phosphatidylcholine (DPPC) which have higher transition temperature compared to normal phospholipids are also known to increase the stability of liposomes by delaying oxidation. In addition, they can also provide controlled release due to the formation of a gel phase below their transition temperature (Han et al., 1997). Though addition of lipids like cholesterol are highly beneficial in drug delivery, they are not preferred in food products due to the association of cholesterol intake with life style diseases like obesity, cardiovascular diseases. As an alternative to cholesterol, phytosterols have been used along with phospholipids for the fabrication of liposomes. Incorporation of phytosterols has shown to increase the encapsulation efficiency of liposomes(Chan et al., 2004).

Encapsulation of bioactives within the liposomes not only avoids the degradation of entrapped bioactives, but in turn, since most of the bioactives like ascorbic acid, anthocyanins, catechin are antioxidants they also inhibit oxidation of lipids which are used in the fabrication of the liposomes(Viljanen et al., 2004). Hence the benefits are

dual. Few examples where liposomes have been utilized to entrap and protect hydrophilic bioactives have been listed in Table1. Though, extensive research has been carried out on entrapment of hydrophobic bioactives using liposomes, their utilization for encapsulation of hydrophilic bioactives is limited.

3.1.3. Lyotropic liquid crystalline nanostructures

These are cubic, hexagonal or lammellar structures formed by the self assembly of mesophasic lipids, collectively known as lyotropic liquid crystal (LLC) systems(Karami and Hamidi, 2016). These structures are formed when liquid crystalline lipid particles are dispersed in the aqueous phase along with stabilizers. These biphasic structures are thermodynamically stable and subsist in equilibrium with excess aqueous phase. The three different types of structures, which can be formed using LLC, are cubic, hexagonal and lamellar.

Cubic liquid crystalline structures are characterized by the presence of bicontinuous domains of water and lipid. Thus this system will be ideal for the delivery of both hydrophilic (in the aqueous domain) and/or hydrophobic (lipid domain) bioactives. In case of hexagonal structures, liquid crystalline lipids are arranged in the form of columns separating the water from within and outside the structure. These structures will be suitable for the delivery of hydrophilic bioactives due to the presence of inner aqueous compartment. In lamellar structures, water channels separate the planar lipid bilayers. Fabrication temperature and/or water content have significant influence on the alignment of lyotropic liquid crystal in the aqueous phase and thus determine the type of the formed structure(Guo et al., 2010).

Glycerol monooleate (GMO) is the most commonly used lipid in the fabrication of LLC using both top-down and bottom-up approach. In top-down approach, liquid-crystal-forming lipid is mixed with surfactant, which is later dispersed within the aqueous phase by applying high energy using high pressure homogenization (HPH), sonication, microfluidization (MF) (Esposito et al., 2003). However in bottom-up approach lipid is solubilized using the hydrotropes and later mixed with the surfactant. Hydrotropes are added to avoid the formation of viscous lipid phase. Later this mixture is dispersed within the aqueous phase with nominal energy input (Spicer et al., 2001). Though, both the approaches results in the formation of liquid crystalline structures, bottom-up approach has several advantages, for example, it requires minimal energy in comparison to top-down approach, system is not exposed to thermal heating caused by the input of high energy and thus it is more suitable for encapsulation of thermosensitive molecules, formed particles are more homogeneous and hence they avoid Ostwald ripening which increases the particle stability(Karami and Hamidi, 2016).

These liquid crystalline nanostructures are tailor made for the delivery of nutraceuticals. For example, they can be fabricated using food grade lipids like GMO, they can be fabricated using industrially feasible and acceptable fabrication methods like HPH, MF and can be used to deliver both hydrophilic and hydrophobic bioactives(Karami and Hamidi, 2016). However, till date no effort has been made to use these nanostructures for the delivery of bioactives, which provides huge opportunity to work towards exploring the possibility of using these structures as nutraceutical delivery vehicles.

3.2. Surfactant Based Carrier Systems

The high cost of lipid ingredients, health concerns associated with the use of lipid in the food products and their limited stability in acidic pH, in presence of bile salts has necessitated the development of alternative delivery systems ideally created using materials, which are cheaper and more stable in wider environmental conditions both in the complex food product and also in the GIT. To meet this challenge, surfactant based delivery systems have been designed e.g. niosomes, bilosomes etc.

3.2.1. Niosomes

Niosomes are vesicles of non-ionic amphiphiles, which form closed bilayer structures (Paecharoenchai et al., 2013). Niosomes are more or less identical to liposomes in terms of their physical properties and formulation procedures. They are also formed either as unilamellar or multilamellar structures (Uchegbu and Vyas, 1998). Niosomes can be used to entrap both hydrophilic and hydrophobic bioactives. Niosomes are less prone for acidic and enzymatic degradation. Hence they are best suited to protect bioactives from acidic and enzymatic degradation in the GIT and acidic food products like beverages (Aditya et al., 2015b; Yoshida et al., 1992). As in liposomes, coating niosomes with polymers like carbopol, chitosan further enhances their stability in acidic condition(Sezgin-Bayindir et al., 2013; Zubairu et al., 2015). In addition, by altering their surface charge, bioavailability and bioaccessibility can be engineered. In one of the study it was found that the negatively charged niosomes are quickly taken up via the Peyer's patches in intestine compared to their positive charged counterparts (Tomizawa et al., 1993). Unfortunately there are only a few research papers published on the use of niosomes for the delivery of hydrophilic bioactives. In one such study, niosomes fabricated using Tween 60 was used to encapsulate hydrophilic bioactives like gallic acid, ascorbic acid along with other hydrophobic bioactives e.g. curcumin, quercetin (co-delivery system). The fabricated system has shown enhanced antioxidant activity and radical scavenging ability due to the controlled release of bioactives and presence of multiple synergistically acting bioactives(Tavano et al., 2014). In another study, niosomes encapsulating (+)-catechin and (−)-epigallocatechin gallate (EGCG) were fabricated by thin film hydration method. Cellular uptake and transport study conducted using human intestinal Caco-2 cells have shown the 2.66- and 2.13-fold higher bioaccessibility and bioavailability (oral bioavailability) compared to their unentrapped counterparts. Further formulation also enhanced the stability of bioactives in the simulated gastrointestinal fluid(Song et al., 2014).

3.2.2. Bilosomes

Bilosomes are modified niosomes. In bilosomes, bile salts are used along with surfactants to form the globular concentric bilayer structures. Some of the bile salts that are generally used to fabricate bilosomes are deoxycholic acid, sodium cholate, deoxycholate, taurocholate etc. Bilosomes are highly stable in the GIT (Katare et al., 2006; Singh et al., 2004). Bile salts are the food grade materials, which are easily available and most commonly used as penetration enhancers to improve the oral bioavailability of vaccine candidates and drug molecules. Though, these structures have been extensively used for the delivery of drug molecules and vaccine candidates, their use in nutraceutical delivery are still not explored. Hence there is a huge opportunity to work towards exploring the possibility of using these structures as nutraceutical delivery vehicles.

3.3. Complexes (Biopolymer particles)

Proteins and polysaccharides carry relatively large number of functional groups which becomes charged under certain environmental conditions e.g. at specific pH, temperature, ionic concentration. By using the interactions that occurs between the oppositely charged macromolecules (protein-polysaccharide or protein-protein), supramolecular structures can be fabricated. These structures can be used for encapsulation and delivery of bioactive compounds. Their natural and inherent essence qualifies them as GRAS materials and therefore makes them suitable for food applications.

The associative interactions that takes place between the macromolecules in the solution are influenced by different physicochemical parameters such as; molecular weight, biopolymer charge density, biopolymer flexibility, total biopolymer concentration, ionic strength, pH, pressure, temperature and shearing (Schmitt and Turgeon, 2011). Formation of complexes by electrostatic complexation generally involves three main steps: the dissolution of biopolymers in the solvent, the mixing of polymers in the required ratio and an acidification step. The acidification step has been shown to have an effect on the formed complex size.

Generally the acidification process is carried out either before mixing two different polymers which is called pre-blending acidification or after mixing the two different polymers which is called as post-blending acidification. Among these two, post-blending acidification is known to produce smaller particles in comparison to pre-blending acidification(Bédié et al., 2008). However, size reduction of the formed particles can be achieved by subjecting them to high shear this overcomes the drawback associated with pre-blending acidification. In this regard, Kurukji *et al*., have successfully reduced the size of the sodium caseinate-chitosan complexes that were fabricated by employing a pre-blending acidification methodology by applying sonication(Kurukji et al., 2016).

Biopolymer nanoparticles have shown to have the properties to encapsulate, protect and deliver bioactive components (minerals, peptides, proteins, enzymes, pharmaceuticals, lipids and dietary fibers). Recently, hydrophilic vitamin B9 was successfully encapsulated in coacervates of two oppositely charged milk proteins beta-lactoglobulin (βlg) and lactoferrin(Chapeau et al., 2015). Additionally, these particles can be used as texturizing agents in formulations. Similarly, catechin was complexed with chitosan to form colloidal particles. This complexation significantly reduced the degradation of catechin within the intestine by avoiding glucuronidation (Zhang and Kosaraju, 2007).

Complexes formed by only electrostatic interactions are prone to dissociation or degradation when surrounding environmental conditions, for example, pH, ionic strength etc., are changed. However, dissociation of complexes due to change in the environmental factors can be used to target and control the release of bioactives at different places in the GIT. Most of complexation process takes place in the low pH (acidic condition). Thus, they will be intact in the acidic pH. Hence these structures are very useful to protect the bioactives in the stomach acidic condition. But after entering the intestine, in the alkaline intestinal pH they dissociate. This will result in release of entrapped bioactives and potentially their absorption(Jones et al., 2010).

If such site-specific delivery is not required, one approach to overcome the limitation of dissociation or degradation is the synthesis of biopolymer nanoparticles using heat denaturation of globular proteins followed by electrostatic complexation with either anionic or cationic polysaccharides. This makes the formed particles more resistant to changes in the environment. Therefore, formation of complexes by heat denaturation

of globular proteins followed by electrostatic complexation is well suited for food application owing to the complex food matrix(Jones et al., 2010).

4. Conclusion

Wide ranges of delivery systems such as liposomes, bilosomes, niosomes, double emulsions, complexes are available that could be used to fortify food products with the desired bioactives. This will enable us to design food products with specific health benefits owing to their specific functionalities. However, to successfully translate lab scale research findings into industrially processed food products, tailor made approach to specifically engineer the particles to suit them to use in heterogeneous food matrix is highly warranted. Further, some of the delivery systems such as bilosomes, niosomes are unexplored for the delivery of nutraceuticals. Hence there requires a proper research effort to explore them as nutraceutical carriers in the future.

Conflicts of interest

The author's declare that they have no competing interests.

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Reference

Aditya, N.P., Aditya, S., Yang, H., Kim, H.W., Park, S.O., Ko, S., 2015a. Co-delivery of hydrophobic curcumin and hydrophilic catechin by a water-in-oil-in-water double emulsion. Food Chemistry 173, 7-13.

Aditya, N.P., Aditya, S., Yang, H.-J., Kim, H.W., Park, S.O., Lee, J., Ko, S., 2015b. Curcumin and catechin co-loaded water-in-oil-in-water emulsion and its beverage application. Journal of Functional Foods 15, 35-43.

Aditya, N.P., Chimote, G., Gunalan, K., Banerjee, R., Patankar, S., Madhusudhan, B., 2012. Curcuminoids-loaded liposomes in combination with arteether protects against Plasmodium berghei infection in mice. Experimental Parasitology 131(3), 292-299.

Aditya, N.P., Ko, S., 2015. Solid lipid nanoparticles (SLNs): delivery vehicles for food bioactives. Rsc Adv 5(39), 30902-30911.

Aditya, N.P., Macedo, A.S., Doktorovova, S., Souto, E.B., Kim, S., Chang, P.-S., Ko, S., 2014. Development and evaluation of lipid nanocarriers for quercetin delivery: A comparative study of solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), and lipid nanoemulsions (LNE). LWT - Food Science and Technology 59(1), 115-121.

Aditya, N.P., Yang, H., Kim, S., Ko, S., 2015c. Fabrication of amorphous curcumin nanosuspensions using β-lactoglobulin to enhance solubility, stability, and bioavailability. Colloids and Surfaces B: Biointerfaces 127, 114-121.

Akbarzadeh, A., Rezaei-Sadabady, R., Davaran, S., Joo, S.W., Zarghami, N., Hanifehpour, Y., Samiei, M., Kouhi, M., Nejati-Koshki, K., 2013. Liposome: classification, preparation, and applications. Nanoscale Research Letters 8(1), 102-102.

Bandyopadhyay, P., Ghosh, A.K., Ghosh, C., 2012. Recent developments on polyphenol-protein interactions: effects on tea and coffee taste, antioxidant properties and the digestive system. Food Funct 3(6), 592-605.

Bédié, G.K., Turgeon, S.L., Makhlouf, J., 2008. Formation of native whey protein isolate–low methoxyl pectin complexes as a matrix for hydro-soluble food ingredient entrapment in acidic foods. Food Hydrocolloids 22(5), 836-844.

Berton-Carabin, C.C., Schroën, K., 2015. Pickering Emulsions for Food Applications: Background, Trends, and Challenges. Annual Review of Food Science and Technology 6(1), 263-297.

Bonnet, M., Cansell, M., Berkaoui, A., Ropers, M.H., Anton, M., Leal-Calderon, F., 2009. Release rate profiles of magnesium from multiple W/O/W emulsions. Food Hydrocolloids 23(1), 92-101.

Bou, R., Cofrades, S., Jiménez-Colmenero, F., 2014. Physicochemical properties and riboflavin encapsulation in double emulsions with different lipid sources. LWT - Food Science and Technology 59(2, Part 1), 621-628.

Chan, Y.H., Chen, B.H., Chiu, C.P., Lu, Y.F., 2004. The influence of phytosterols on the encapsulation efficiency of cholesterol liposomes. Int J Food Sci Tech 39(9), 985-995.

Chapeau, A.-L., Miranda-Tavares, G., Hamon, P., Croguennec, T., Bouhallab, S., Poncelet, D., 2015. Spontaneous co-assembly of proteins for encapsulation of a hydrophilic vitamin, 23.International Conference on Bioencapsulation. Delft, Netherlands, p. np.

Chen, H., Langer, R., 1998. Oral particulate delivery: status and future trends. Advanced drug delivery reviews 34(2-3), 339-350.

Cheynier, V., 2005. Polyphenols in foods are more complex than often thought. The American Journal of Clinical Nutrition 81(1), 223S-229S.

Day, L., Seymour, R.B., Pitts, K.F., Konczak, I., Lundin, L., 2009. Incorporation of functional ingredients into foods. Trends in Food Science & Technology 20(9), 388-395.

Dickinson, E., 2015a. Colloids in Food: Ingredients, Structure, and Stability. Annual Review of Food Science and Technology 6(1), 211-233.

Dickinson, E., 2015b. Microgels — An alternative colloidal ingredient for stabilization of food emulsions. Trends in Food Science & Technology 43(2), 178-188.

Drewnowski, A., Gomez-Carneros, C., 2000. Bitter taste, phytonutrients, and the consumer: a review. Am J Clin Nutr 72(6), 1424-1435.

Esposito, E., Eblovi, N., Rasi, S., Drechsler, M., Di Gregorio, G.M., Menegatti, E., Cortesi, R., 2003. Lipid-based supramolecular systems for topical application: a preformulatory study. AAPS PharmSci 5(4), E30.

Fang, Z., Bhandari, B., 2012. 4 - Spray drying, freeze drying and related processes for food ingredient and nutraceutical encapsulation, in: Garti, N., McClements, D.J. (Eds.), Encapsulation Technologies and Delivery Systems for Food Ingredients and Nutraceuticals. Woodhead Publishing, pp. 73-109.

Farhang, B., Kakuda, Y., Corredig, M., 2012. Encapsulation of ascorbic acid in liposomes prepared with milk fat globule membrane-derived phospholipids. Dairy Sci Technol 92(4), 353-366.

Fathi, M., Mozafari, M.R., Mohebbi, M., 2012. Nanoencapsulation of food ingredients using lipid based delivery systems. Trends in Food Science & Technology 23(1), 13-27.

Frasch-Melnik, S., Spyropoulos, F., Norton, I.T., 2010. W1/O/W2 double emulsions stabilised by fat crystals – Formulation, stability and salt release. Journal of Colloid and Interface Science 350(1), 178-185.

Garrec, D.A., Frasch-Melnik, S., Henry, J.V.L., Spyropoulos, F., Norton, I.T., 2012. Designing colloidal structures for micro and macro nutrient content and release in foods. Faraday Discussions 158(0), 37-49.

Gibbs, B.F., Kermasha, S., Alli, I., Mulligan, C.N., 1999. Encapsulation in the food industry: a review. Int J Food Sci Nutr 50(3), 213-224.

Giroux, H.J., Constantineau, S., Fustier, P., Champagne, C.P., St-Gelais, D., Lacroix, M., Britten, M., 2013. Cheese fortification using water-in-oil-in-water double emulsions as carrier for water soluble nutrients. International Dairy Journal 29(2), 107-114.

Gregersen, S.B., Miller, R.L., Hammershøj, M., Andersen, M.D., Wiking, L., 2015. Texture and microstructure of cocoa butter replacers: Influence of composition and cooling rate. Food Structure 4, 2-15.

Guo, C., Wang, J., Cao, F., Lee, R.J., Zhai, G., 2010. Lyotropic liquid crystal systems in drug delivery. Drug Discov Today 15(23-24), 1032-1040.

Han, M., Watarai, S., Kobayashi, K., Yasuda, T., 1997. Application of liposomes for development of oral vaccines: study of in vitro stability of liposomes and antibody response to antigen associated with liposomes after oral immunization. The Journal of veterinary medical science / the Japanese Society of Veterinary Science 59(12), 1109-1114.

Hussain, N., Jaitley, V., Florence, A.T., 2001. Recent advances in the understanding of uptake of microparticulates across the gastrointestinal lymphatics. Advanced drug delivery reviews 50(1-2), 107-142.

Janaswamy, S., Youngren, S.R., 2012. Hydrocolloid-based nutraceutical delivery systems. Food Funct 3(5), 503-507.

Jones, O.G., Lesmes, U., Dubin, P., McClements, D.J., 2010. Effect of polysaccharide charge on formation and properties of biopolymer nanoparticles created by heat treatment of β-lactoglobulin–pectin complexes. Food Hydrocolloids 24(4), 374-383.

Karami, Z., Hamidi, M., 2016. Cubosomes: remarkable drug delivery potential. Drug Discovery Today 21(5), 789-801.

Karewicz, A., Bielska, D., Loboda, A., Gzyl-Malcher, B., Bednar, J., Jozkowicz, A., Dulak, J., Nowakowska, M., 2013. Curcumin-containing liposomes stabilized by thin layers of chitosan derivatives. Colloids and Surfaces B: Biointerfaces 109, 307-316.

Katare, R., Gupta, P.N., Mahor, S., Rawat, A., Khatri, K., Katare, Y., Panda, A.K., Vyas, S.P., 2006. Development of polysaccharide-capped niosomes for oral immunization of tetanus toxoid. J Drug Deliv Sci Tec 16(3), 167-172.

Kirby, C.J., Whittle, C.J., Rigby, N., Coxon, D.T., Law, B.A., 1991. Stabilization of ascorbic acid by microencapsulation in liposomes. International Journal of Food Science & Technology 26(5), 437-449.

Kurukji, D., Norton, I., Spyropoulos, F., 2016. Fabrication of sub-micron protein-chitosan electrostatic complexes for encapsulation and pH-Modulated delivery of model hydrophilic active compounds. Food Hydrocolloids 53, 249-260.

Lad, M., Hewson, L., Wolf, B., 2012. Enhancing saltiness in emulsion based foods. Flavour 1(1), 13.

Lam, S., Velikov, K.P., Velev, O.D., 2014. Pickering stabilization of foams and emulsions with particles of biological origin. Current Opinion in Colloid & Interface Science 19(5), 490-500.

Lee, J.-S., Chung, D., Lee, H.G., 2008. Preparation and characterization of calcium pectinate gel beads entrapping catechin-loaded liposomes. International Journal of Biological Macromolecules 42(2), 178-184.

Lian, T., Ho, R.J.Y., 2001. Trends and developments in liposome drug delivery systems. J Pharm Sci 90(6), 667-680.

Mady, M.M., Darwish, M.M., 2010. Effect of chitosan coating on the characteristics of DPPC liposomes. Journal of Advanced Research 1(3), 187-191.

McClements, D.J., 2015. Encapsulation, protection, and release of hydrophilic active components: Potential and limitations of colloidal delivery systems. Adv Colloid Interfac 219, 27-53.

McClements, D.J., Decker, E.A., Park, Y., Weiss, J., 2009. Structural Design Principles for Delivery of Bioactive Components in Nutraceuticals and Functional Foods. Crit Rev Food Sci 49(6), 577-606.

McClements, D.J., Saliva-Trujillo, L., Zhang, R., Zhang, Z., Zou, L., Yao, M., Xiao, H., 2016. Boosting the bioavailability of hydrophobic nutrients, vitamins, and nutraceuticals in natural products using excipient emulsions. Food Research International 88, 140–152.

McClements, D.J., Xiao, H., 2014. Excipient foods: designing food matrices that improve the oral bioavailability of pharmaceuticals and nutraceuticals. Food Funct 5(7), 1320-1333.

McIntosh, T.J., Simon, S.A., Vierling, P., Santaella, C., Ravily, V., 1996. Structure and interactive properties of highly fluorinated phospholipid bilayers. Biophys J 71(4), 1853-1868.

Mirafzali, Z., Thompson, C.S., Tallua, K., 2014. Chapter 13 - Application of Liposomes in the Food Industry A2 - Gaonkar, Anilkumar G, in: Vasisht, N., Khare, A.R., Sobel, R. (Eds.), Microencapsulation in the Food Industry. Academic Press, San Diego, pp. 139-150.

Norton, J.E., Espinosa, Y.G., Watson, R.L., Spyropoulos, F., Norton, I.T., 2015. Functional food microstructures for macronutrient release and delivery. Food Funct 6(3), 663-678.

Paecharoenchai, O., Teng, L., Yung, B.C., Teng, L., Opanasopit, P., Lee, R.J., 2013. Nonionic surfactant vesicles for delivery of RNAi therapeutics. Nanomedicine (Lond) 8(11), 1865-1873.

Patel, A.R., Velikov, K.P., 2011. Colloidal delivery systems in foods: A general comparison with oral drug delivery. Lwt-Food Sci Technol 44(9), 1958-1964.

Pimentel-González, D.J., Campos-Montiel, R.G., Lobato-Calleros, C., Pedroza-Islas, R., Vernon-Carter, E.J., 2009. Encapsulation of Lactobacillus rhamnosus in double emulsions formulated with sweet whey as emulsifier and survival in simulated gastrointestinal conditions. Food Research International 42(2), 292-297.

Raoufi, N., Tehrani, M.M., Farhoosh, R., Golmohammadzadeh, S., 2012. The effects of adding water and polyglycerol polyricinoleate on the texture, appearance, and sensory qualities of compound milk chocolate. European Journal of Lipid Science and Technology 114(12), 1390-1399.

Rashidinejad, A., Birch, E.J., Sun-Waterhouse, D., Everett, D.W., 2014. Delivery of green tea catechin and epigallocatechin gallate in liposomes incorporated into low-fat hard cheese. Food Chemistry 156, 176-183.

Reineccius, G.A., 1995. Liposomes for Controlled-Release in the Food-Industry. Acs Sym Ser 590, 113-131.

Rodríguez-Nogales, J.M., López, A.D., 2006. A novel approach to develop β-galactosidase entrapped in liposomes in order to prevent an immediate hydrolysis of lactose in milk. International Dairy Journal 16(4), 354-360.

Rothwell, J.A., Medina-Remón, A., Pérez-Jiménez, J., Neveu, V., Knaze, V., Slimani, N., Scalbert, A., 2015. Effects of food processing on polyphenol contents: A systematic analysis using Phenol-Explorer data. Molecular Nutrition & Food Research 59(1), 160-170.

Saha, D., Bhattacharya, S., 2010. Hydrocolloids as thickening and gelling agents in food: a critical review. Journal of food science and technology 47(6), 587-597.

Santos, M.G., Bozza, F.T., Thomazini, M., Favaro-Trindade, C.S., 2015. Microencapsulation of xylitol by double emulsion followed by complex coacervation. Food Chemistry 171, 32-39.

Schmitt, C., Turgeon, S.L., 2011. Protein/polysaccharide complexes and coacervates in food systems. Advances in Colloid and Interface Science 167(1–2), 63-70.

Sezgin-Bayindir, Z., Onay-Besikci, A., Vural, N., Yuksel, N., 2013. Niosomes encapsulating paclitaxel for oral bioavailability enhancement: preparation, characterization, pharmacokinetics and biodistribution. J Microencapsul 30(8), 796-804.

Shewan, H.M., Stokes, J.R., 2013. Review of techniques to manufacture micro-hydrogel particles for the food industry and their applications. Journal of Food Engineering 119(4), 781-792.

Shoba, G., Joy, D., Joseph, T., Majeed, M., Rajendran, R., Srinivas, P.S., 1998. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. Planta Med 64(4), 353-356.

Singh, H., Thompson, A., Liu, W., Corredig, M., 2012. 11 - Liposomes as food ingredients and nutraceutical delivery systems A2 - Garti, Nissim, in: McClements, D.J. (Ed.) Encapsulation Technologies and Delivery Systems for Food Ingredients and Nutraceuticals. Woodhead Publishing, pp. 287-318.

Singh, P., Prabakaran, D., Jain, S., Mishra, V., Jaganathan, K., Vyas, S.P., 2004. Cholera toxin B subunit conjugated bile salt stabilized vesicles (bilosomes) for oral immunization. International journal of pharmaceutics 278(2), 379-390.

Smith, M.R., Wilson, R., Hepburn, P.A., 1998. Assessment of the Carcinogenic Potential of Polyglycerol Polyricinoleate (PGPR) in Rats and Mice. Food and Chemical Toxicology 36(9–10), 747-754.

Smuda, M., Glomb, M.A., 2013. Maillard Degradation Pathways of Vitamin C. Angewandte Chemie International Edition 52(18), 4887-4891.

Song, Q., Li, D., Zhou, Y., Yang, J., Yang, W., Zhou, G., Wen, J., 2014. Enhanced uptake and transport of (+)-catechin and (-)-epigallocatechin gallate in niosomal formulation by human intestinal Caco-2 cells. Int J Nanomedicine 9, 2157-2165.

Spicer, P.T., Hayden, K.L., Lynch, M.L., Ofori-Boateng, A., Burns, J.L., 2001. Novel Process for Producing Cubic Liquid Crystalline Nanoparticles (Cubosomes). Langmuir 17(19), 5748-5756.

Tavano, L., Muzzalupo, R., Picci, N., de Cindio, B., 2014. Co-encapsulation of antioxidants into niosomal carriers: Gastrointestinal release studies for nutraceutical applications. Colloids and Surfaces B: Biointerfaces 114, 82-88.

Tomizawa, H., Aramaki, Y., Fujii, Y., Kara, T., Suzuki, N., Yachi, K., Kikuchi, H., Tsuchiya, S., 1993. Uptake of phosphatidylserine liposomes by rat Peyer's patches following intraluminal administration. Pharmaceutical research 10(4), 549-552.

Uchegbu, I.F., Vyas, S.P., 1998. Non-ionic surfactant based vesicles (niosomes) in drug delivery. International journal of pharmaceutics 172(1), 33-70.

Velikov, K.P., Pelan, E., 2008. Colloidal delivery systems for micronutrients and nutraceuticals. Soft Matter 4(10), 1964-1980.

Venugopal, V., 2008. Marine Nutraceuticals for Food Fortification and Enrichment, Marine Products for Healthcare. CRC Press, pp. 405-428.

Viljanen, K., Kylli, P., Kivikari, R., Heinonen, M., 2004. Inhibition of Protein and Lipid Oxidation in Liposomes by Berry Phenolics. Journal of Agricultural and Food Chemistry 52(24), 7419-7424.

Wang, R., Zhou, W., Jiang, X., 2008. Reaction kinetics of degradation and epimerization of epigallocatechin gallate (EGCG) in aqueous system over a wide temperature range. J Agric Food Chem 56(8), 2694-2701.

Watwe, R.M., Bellare, J.R., 1995. Manufacture of Liposomes - a Review. Curr Sci India 68(7), 715-724.

Wilson, R., van Schie, B.J., Howes, D., 1998. Overview of the Preparation, Use and Biological Studies on Polyglycerol Polyricinoleate (PGPR). Food and Chemical Toxicology 36(9–10), 711-718.

Xia, S., Xu, S., 2005. Ferrous sulfate liposomes: preparation, stability and application in fluid milk. Food Research International 38(3), 289-296.

Yao, M.F., McClements, D.J., Xiao, H., 2015. Improving oral bioavailability of nutraceuticals by engineered nanoparticle-based delivery systems. Curr Opin Food Sci 2, 14-19.

Yi, O.-S., Meyer, A.S., Frankel, E.N., 1997. Antioxidant activity of grape extracts in a lecithin liposome system. Journal of the American Oil Chemists' Society 74(10), 1301-1307.

Yoshida, H., Lehr, C.-M., Kok, W., Junginger, H., Verhoef, J., Bouwstra, J., 1992. Niosomes for oral delivery of peptide drugs. Journal of Controlled Release 21(1), 145-153.

Zhang, L.Y., Kosaraju, S.L., 2007. Biopolymeric delivery system for controlled release of polyphenolic antioxidants. Eur Polym J 43(7), 2956-2966.

Zhu, C.F., Sanahuja, G., Yuan, D.W., Farre, G., Arjo, G., Berman, J., Zorrilla-Lopez, U., Banakar, R., Bai, C., Perez-Massot, E., Bassie, L., Capell, T., Christou, P., 2013. Biofortification of plants with altered antioxidant content and composition: genetic engineering strategies. Plant Biotechnol J 11(2), 129-141.

Zorić, Z., Pedisić, S., Kovačević, D.B., Ježek, D., Dragović-Uzelac, V., 2016. Impact of packaging material and storage conditions on polyphenol stability, colour and sensory characteristics of freeze-dried sour cherry (prunus cerasus var. Marasca). Journal of Food Science and Technology 53(2), 1247-1258.

Zubairu, Y., Negi, L.M., Iqbal, Z., Talegaonkar, S., 2015. Design and development of novel bioadhesive niosomal formulation for the transcorneal delivery of anti-infective agent: In-vitro and ex-vivo investigations. Asian Journal of Pharmaceutical Sciences 10(4), 322-330.

Table1. Hydrophilic bioactives entrapped liposome formulations.

Bioactives	Fabrication method	Result/outcome	Reference
Ascorbic acid	Thin film hydration	Increased aqueous stability	(Kirby et al., 1991)
Ascorbic acid	Microfluidization	Increased aqueous stability	(Farhang et al., 2012)
Catechin	Thin film hydration	Controlled release	(Lee et al., 2008)
Catechin	Mechanical agitation	Enhanced stability in product (cheese)	(Rashidinejad et al., 2014)
β-galactosidase	Thin film hydration	Inhibition of hydrolysis in milk	(Rodríguez-Nogales and López, 2006)
Ferrous Sulphate∗	Reverse phase evaporation	Increased thermal and aqueous stability	(Xia and Xu, 2005)
Anthocyanins	Sonication	Inhibit lipid oxidation	(Viljanen et al., 2004)
Gallic acid∗	Thin film hydration	Enhanced antioxidant activity	(Yi et al., 1997)

∗ Compounds those are fairly soluble in water.

List of figures

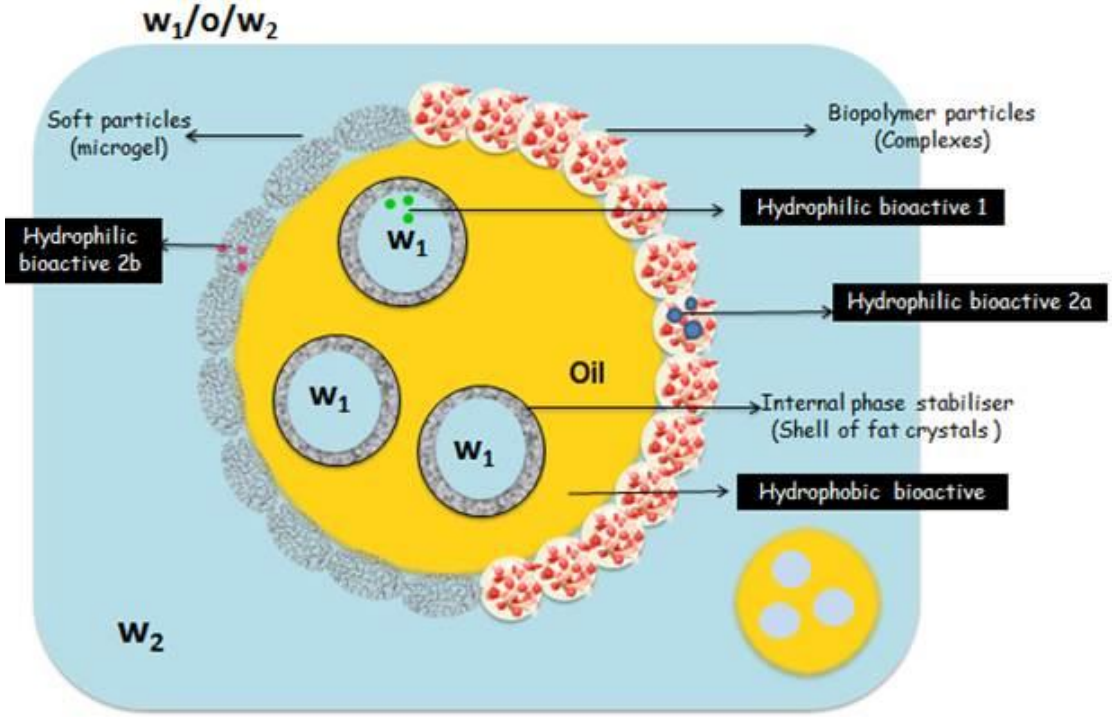

Figure 1.

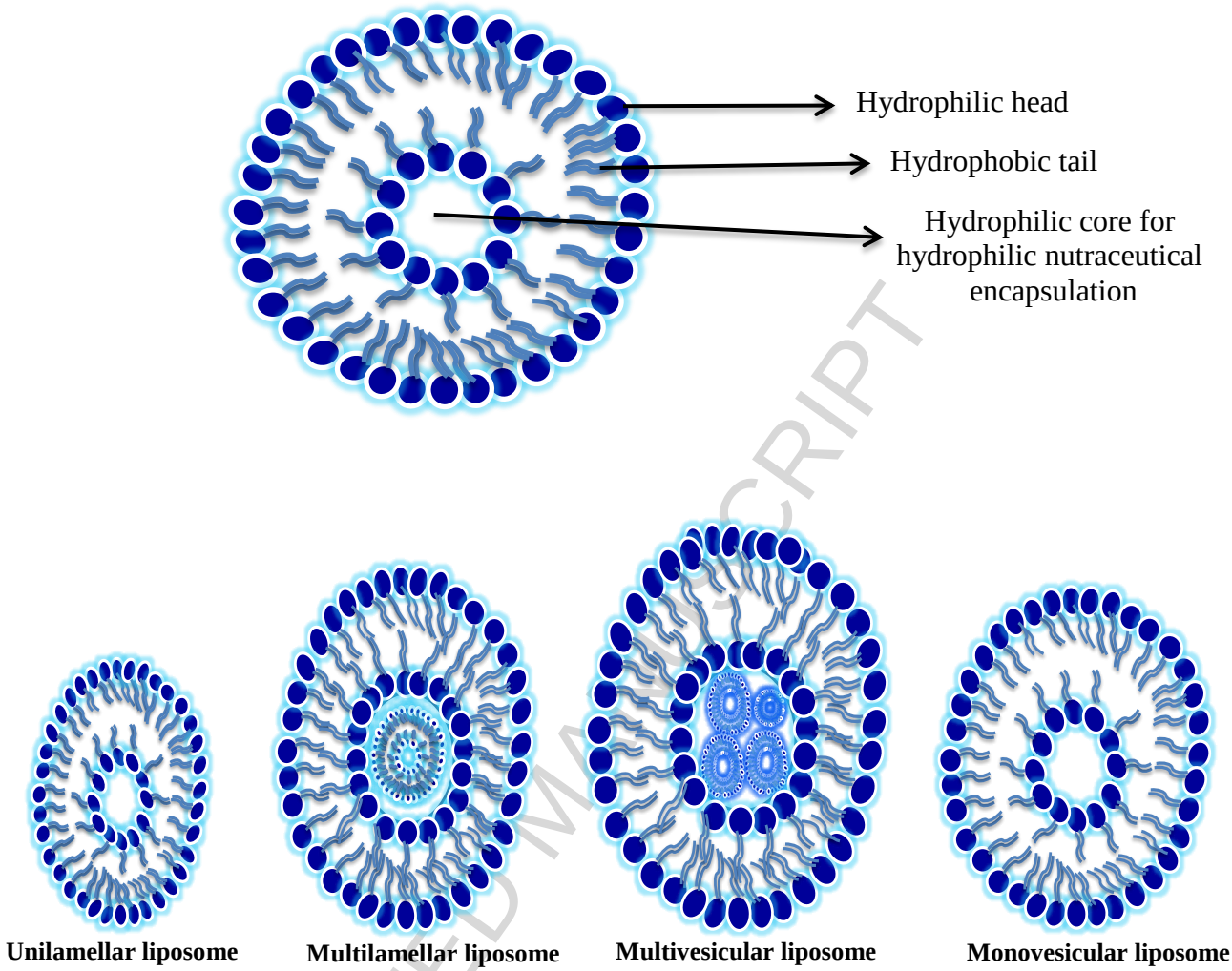

Figure 2.